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SECOND SERIES VOL. X, No. 2

BULLETIN

OF

THE NEW YORK ACADEMY OF MEDICINE

INCORPORATED 1851

FEBRUARY, 1934

PUBLISHED MONTHLY BY

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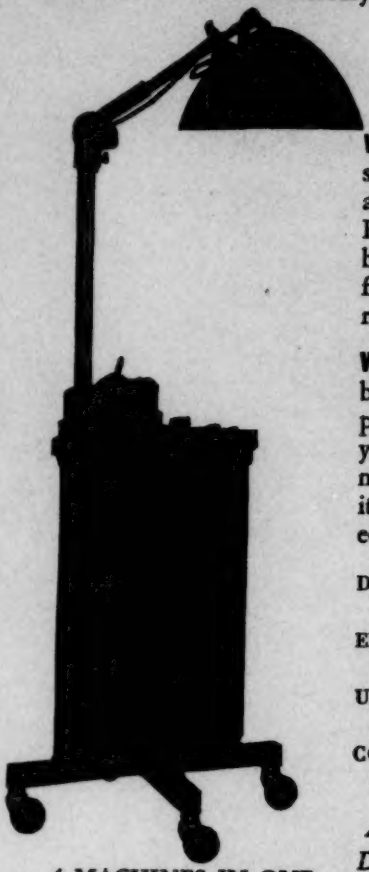

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BULLETIN OF
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VOL. X FEBRUARY, 1934 No. 2

LINSLY RUDD WILLIAMS

The Council at its regular meeting on January 24 voted to hold a memorial service to Dr. Williams in Hosack Hall at a date to be announced later, the arrangements for which are to be placed in the hands of a special committee.

It is planned that the speakers at this meeting will represent the various activities of Dr. Williams' many-sided life.

The Council further voted that a special volume shall be published by the Academy as a memorial to Dr. Williams in which will appear the resolutions adopted by the Council, the various Committees of the Academy and other organizations, the addresses delivered at the memorial service, and other contributions.

ANNUAL GRADUATE FORTNIGHT
"DISORDERS OF METABOLISM"
October 23 to November 3, 1933

METABOLISM IN HYPERTHYROIDISM AND HYPOTHYROIDISM*

WALTER WALKER PALMER

A comprehensive review of the field of metabolism in diseases of the thyroid gland is obviously an impossible task in the brief space at our disposal, nor would it serve the purpose for which these gatherings are designed. During the past two decades the interest of the physiologists and physicians in the subject has resulted in numerous investigations which have brought forth now well established facts of great value to the practitioner. The purpose of this talk is to consider some of the practical problems in the diagnosis and management of diseases of the thyroid in so far as alterations in metabolism are concerned.

By far the most common diseases of the thyroid are believed to be due to either diminished or increased activity of the gland, in its elaboration and discharge into the general circulation of the hormone thyroglobulin. Of the thyroid insufficiencies, myxedema in adults and cretinism in children are easily recognized clinically. The diffuse symmetrical enlargements of the thyroid gland at puberty and in the low iodine areas are associated with a slight insufficiency. All conditions in which there is over-activity are usually designated as hyperthyroidism, "toxic thyroids" or exophthalmic goiter. Fortunately malignant disease of the thyroid is much less common as is also acute and chronic thyroiditis.

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* Delivered October 24, 1933.

Basal Metabolism

The level of the basal metabolism is now recognized by both physiologists and clinicians as one of the best indications of the activity of the thyroid gland. As early as 1893 Friedrich Müller called attention to the emaciation and loss of weight in spite of the high caloric intake in exophthalmic goiter patients which suggested to him that the total metabolism was increased in this disease. By 1897 Magnus-Levy had demonstrated an increased oxygen consumption in hyperthyroidism, and diminished oxygen consumption in cretinism and myxedema. It was not until 1912 that the work at the Russell Sage Institute of Pathology and Carnegie Nutrition Laboratory provided us with an apparatus and method for the determination of basal metabolism which was suitable for clinical purposes. Since then the apparatus has been simplified and improved so that at the present time basal metabolism determinations have become a part of the routine in all well organized clinics and many doctors' offices. As a test of thyroid activity basal metabolism determinations have proved of great value in diagnosis and treatment of the diseases of the thyroid gland. There are, however, certain limitations of a laboratory test of this type. The technic, while not particularly difficult, is full of pitfalls which may lead to errors amounting to 10 or even 20 per cent. The normal standards in general use are for most purposes adequate, but it should be remembered that an occasional normal individual may have a basal metabolism well outside the range set as normal for the test. The diet and state of nutrition are important. In the under nourished the metabolism is lower while in the well nourished it may be elevated. The state of mind, the trained versus the untrained subject, the muscular tone are all factors necessary of consideration in slight or moderate variations from the normal mean. While there may be a tendency for errors in different directions to neutralize one another there is always a possibility of a combination tending to a large discrepancy in a single instance. In certain diseases

there are well recognized variations from normal. A slightly elevated metabolism is frequently found in hypertension, malignancy, pregnancy, acromegaly, leukemias, polycythemia and infections. On the other hand, a lowered basal metabolism may be present in the anemias, Addison's disease, many skin diseases, tumors of the pituitary gland and in diabetes.

Thyroid Insufficiencies

The physician receives little help in identifying myxedema or cretinism from basal metabolism determinations. The clinical picture is characteristic and unmistakable. The B.M.R. is usually 30 per cent or more below the normal average. A B.M.R. of —40 per cent is considered to indicate a total lack of thyroid activity although as low as —59 per cent has been reported. Supplying the needed hormone by the administration of one of the several thyroid preparations can be successfully and safely carried out if reasonable care be exercised. A certain comfort, however, is derived from following the effect of treatment with basal metabolic rates. Inconsistencies between the clinical picture and the B.M.R. do occur as the following case will illustrate. An unmarried woman of 35 presented a classical picture of myxedema. Repeated B.M.R. determinations were within normal limits, the lowest value being —11 per cent. Subsequent experience revealed the fact that with six grains daily of the Burroughs Wellcome preparation all signs and symptoms of myxedema disappeared although the B.M.R. never went above +6 per cent, except on one occasion when the patient on her own account increased the daily intake to eight grains. After two weeks she developed outspoken symptoms of hyperthyroidism, nervousness, sweating, and a rapid pulse. Her basal at this time was +19 per cent.

Situations more confusing and difficult are those met in patients with a low B.M.R. without the clinical features of myxedema. Some of these patients unquestionably have a diminished thyroid activity and are markedly improved

following the administration of thyroid substance sufficient to bring their B.M.R. to within the normal range. Others either have a low B.M.R. normally or are suffering from disturbances other than within the thyroid gland. The administration of thyroid gland as a therapeutic test is probably the best method of differentiating these cases. In addition to the effect on the clinical condition the B.M.R. control is of great advantage. Thyroid gland should be given in amounts sufficient to bring the B.M.R. to within normal limits. Occasionally the result is spectacular and improvement is striking. In other cases without any change in the B.M.R. the patient may complain of accentuation of existing symptoms and no clinical benefit result. Still others with large doses of thyroid extract no beneficial change is observed in the clinical picture nor is there the expected rise in B.M.R. Carefully controlled administration of thyroxin by mouth or parenterally may be tried. The low B.M.R. in our experience is encountered most frequently among those patients who complain of nervousness, easy fatigueability, sensitivity to cold and menstrual disorders. They are usually individuals who are worried over their ability to maintain a satisfactory social or economic position in the community; lack force of character; have a low blood pressure; and are poor physical specimens. As a rule their B.M.R. is seldom lower than —20 per cent and it is in this group that thyroid gland therapy is most disappointing. A small percentage of patients apparently exhibit what seems to be a true hypothyroidism, the B.M.R. is usually as low as —25 per cent or lower and they improve with thyroid gland administration.

The adolescent goiter is associated probably with slight insufficiency. Frequently the girls have a B.M.R. between —15 and —20 per cent. The normal variation of the B.M.R. among youths of the adolescent age is greater than among adults, frequently on the low side. Most of the individuals with adolescent goiter living outside the endemic goiter areas probably need little treatment. It is our practice, however, following the advice of Marine, to administer

small doses of thyroid substance (Burroughs Wellcome Co.) gr. ii daily for two weeks, and, after two weeks' rest, iodine in the form of syrup of hydriodic acid, 30 minims daily for two weeks. This regime is carried out three or four times a year. If no change in the size of the gland occurs within a year or at least two years there is little likelihood such measures will result in any change. In our experience of several years at the Presbyterian Hospital it must be said that only an occasional instance of significant reduction in the size of the gland has been observed. This apparently is contrary to the experience of physicians practicing in the endemic areas where iodine administration is usually followed by a reduction in the size of the gland. A few patients of this type have come to us who have been given sufficient thyroid extract to produce a true exophthalmic goiter, a therapeutic procedure which cannot be too strongly condemned.

Hyperthyroidism

As in thyroid deficiency the B.M.R. aids the clinician but little in the diagnosis of clear cut cases of hyperthyroidism. The test is of service in following the course of treatment be it medical or surgical. There is a temptation on the part of physicians to lean too heavily on this test. The wise clinician will place equal importance upon the course of the disease clinically. It is perhaps most useful in judging the optimum effect of iodine administration in preparation for operation and following the effect of radiotherapy.

Occasionally patients are seen where there appears to be wide discrepancies between the basal metabolism and the clinical impression. In one patient A. L. (258530) a housewife of 57 entered the dispensary June 3, 1930, with the sole complaint of constipation. The physical examination revealed little except an elevated blood pressure 210/110 and a secondary anemia (Hgb. 58, RBC 3,200,000). After six months' observation with liberal doses of iron ammonium citrate the blood improved (Hgb. 78, RBC 4,400,000) but little progress was made with relief of

constipation. The B.M.R. at this time was +38 per cent without any discoverable signs or symptoms of hyperthyroidism. Two months later the B.M.R. was +59 per cent. After iodine administration the B.M.R. fell to —5 and —1 per cent with relief of constipation and a general betterment in sense of well being. In this case it may reasonably be assumed we were dealing with hyperthyroidism which would have escaped without the aid of the B.M.R.

As opposed to the above case is A. K. (378839) a woman of 34 admitted to the clinic May 18, 1933, complaining of nervousness following a stillbirth three years ago with a marked increase in symptoms during the past year and a loss of 27 pounds. Clinically there seemed to be no question of the diagnosis of hyperthyroidism. There was a distinct stare without exophthalmos, edema of the eyelids, a moderate symmetrical enlargement of the thyroid gland, an over-acting heart with a rate of 96, and a fine tremor of the fingers. Contrary to expectations the B.M.R. was only +14 per cent. Because of the mild grade of the symptoms, the slight enlargement of the thyroid gland and undoubtedly influenced by the low B.M.R. it was decided to try radiotherapy. Treatments were given three weeks apart. After the third treatment the B.M.R. was +32 per cent, and after the fifth +51 per cent, although clinically she has shown steady improvement. She is still under treatment and we anticipate the B.M.R. will fall.

Another patient illustrates the lack of parallelism between the B.M.R. and clinical impression. O.F. (264282) a colored domestic, age 43, widow, came under our observation July 24, 1930, with unmistakable hyperthyroidism clinically supported by the B.M.R. which was +55 per cent. Her B.M.R. determinations are reported in detail.

Date	B. M. R.	Pulse	Remarks
July 24, 1930	+55	80	Seen in O. P. D. Operation delayed at patient's request.
August 19, 1930	+50	84	Admitted to hospital August 17. Sodium iodide 0.1 gm. daily started.

August	26, 1930	+51	100	Sod. iodide increased to 0.2 daily.
September	3, 1930	+94	108	Good clinical improvement. Sod.
September	4, 1930	+84	92	iodide discontinued. Lugol's 2 mils daily.
September	9, 1930	+40	108	Partial thyroidectomy September 10, 1930.
September	18, 1930	+22	100	Made an excellent convalescence from operation.
September	22, 1930	+26	80	Discharged from hospital.
February	27, 1931			Gained weight and doing housework. Not nervous, no palpitation or tremor.
August	21, 1931	+65	76	No evidence of hyperthyroidism.
November	21, 1931	+68	88	No symptoms of hyperthyroidism.
August	19, 1932	+46	72	No discoverable enlargement of remnant of thyroid gland.
August	4, 1933	+40	68	Continued in excellent condition.

Were it not for the consistency of the several B.M.R. determinations, the accuracy of the observation might be challenged. There is a striking lack of correspondence between the B.M.R. and clinical condition. This case further illustrates the occasional lack of correlation between the pulse rate and B.M.R.

Heart Disease

Since the introduction of basal metabolism determinations into clinical use a real advance has been made in bringing to light cases of hyperthyroidism masquerading as heart disease. The test has served to improve the keenness of the clinical eye. Many of the patients in this category have few or no discoverable signs of hyperthyroidism and appear to be suffering solely from heart disease. The patient is usually over forty, frequently fibrillating, with unmistakable evidence of cardiac failure. There is no exophthalmos, no enlargement of the thyroid gland, no nervousness, profuse perspiration or tremor yet the B.M.R. may be markedly elevated. Attention may be drawn to these cases by the poor response to digitalization. Following partial thyroidectomy the clinical improvement leaves no doubt as to the correctness of the diagnosis.

Furthermore the pathological laboratory demonstrates a hyperactive gland on microscopic examination. As an illustration of this condition the following case is reported. L.B. (358799), 47, single woman, in domestic service entered the hospital October 20, 1932, complaining of dyspnea, palpitation, nervousness and insomnia. Her palms were not moist, there was no exophthalmos; the thyroid gland was moderately enlarged; the heart was enlarged with unmistakable signs of mitral stenosis, the rate was rapid and totally irregular. The diagnosis was rheumatic heart disease, mitral stenosis and fibrillation, with a debatable element of hyperthyroidism since she had an enlarged thyroid and a B.M.R. of +25 per cent. Several weeks of rest with digitalis resulted in no marked improvement. A partial thyroidectomy was performed following which the cardiac situation improved rapidly. Six months after operation there were no cardiac symptoms although she was still fibrillating without pulse deficit.

Another case—L.C. (367468), a Chinaman of 57 entered the hospital January 1, 1933, complaining of swollen legs, palpitation, dyspnea and cough with occasionally blood streaked sputum of three months' duration. He was an apathetic individual distinctly icteric, not suggesting hyperthyroidism in the least. The thyroid gland was slightly enlarged and possibly a slight stare noted in the eyes but no exophthalmos. His heart was large, without organic valvular disease, rate rapid and regular: His liver enlarged and tender: Edema of the lower legs. He was considered to be a case of arteriosclerotic heart disease. On rest and digitalis for several weeks no significant improvement was made. A basal metabolism determination was made and found to be +52 per cent. Partial thyroidectomy was followed by slow but distinct improvement, the jaundice cleared and signs of cardiac decompensation disappeared. He left for China April 10.

The extraordinary benefit derived from partial thyroidectomy in patients similar to these just described has led Blumgart and Levine to reduce the level of metabolism in

individuals with chronic heart disease but without hyperthyroidism by total ablation of the thyroid gland. Several cases are reported and the results give much promise. The period of observation has been too short to permit any definite statement concerning the advisability of so revolutionary a procedure.

One of the difficult problems with which the physician is frequently confronted is the differential diagnosis between psychoneurosis and hyperthyroidism. In many psychoneurotics the clinical picture is suggestive of hyperthyroidism. There may be a B.M.R. of +15 to +20 per cent. Each patient presents a particular situation and I know of no scheme by which a separation can be made with certainty. Without doubt many individuals have lost part of their thyroid gland unnecessarily and probably others have missed the opportunity of relief by operation. A large number of patients assigned to the group of psychoneurotics have normal B.M.R. so that any marked increase in basal should be viewed with suspicion. When doubt exists the patient with moderately increased basal should be closely observed in good circumstances, with rest and sedatives and frequent B.M.R.s made to determine its persistence. In certain of these cases the effect of iodine on the basal is of considerable diagnostic aid. If the B.M.R. be lowered following the administration of iodine then iodine should be discontinued to determine whether the basal is to return to its original level. A repetition of the experiment is desirable. A drop in the B.M.R. with clinical improvement following iodine administration is certainly suggestive of hyperthyroidism. On the other hand when no reduction of the basal is observed in such a procedure we consider the evidence in favor of the absence of hyperthyroidism.

Malignant Disease and Thyroiditis

The basal metabolic rate is of little aid in the diagnosis of malignant disease of the thyroid. Of twenty-four cases reviewed at the Presbyterian Hospital there were B.M.R.

determined on twelve. In eight cases the basal was within normal limits, the remaining —17 and —23 per cent, +39 and +80 per cent. The same may be said of acute and chronic thyroiditis. All of the basals in the few cases we have observed, eight in all, have been within normal limits.

General Metabolic Considerations

The effect of hyperthyroidism or hypothyroidism on the protein, carbohydrate and fat metabolism can be explained largely, if not wholly, on the basis of the increased or decreased level of heat production. With adequate fat and carbohydrate, protein minima correspond to those found in normals. There appears to be no difficulty in the utilization of carbohydrate on the part of the hyperthyroid and the inability to store it is due to the increased demand for food. It has been observed that the cholesterol in the blood is increased in hypothyroidism and decreased in hyperthyroidism. This fact is considered by Hurxthal of value as a differential diagnostic aid in puzzling cases but I have had no personal experience with it.

The enormous increase in heat production in hyperthyroidism means that an increased amount of food is needed for the patient. We hear the "high caloric diet" mentioned frequently in connection with the treatment of hyperthyroidism either surgically or medically. Many times the so-called high caloric diet as prescribed is inadequate. Numerous observations now confirm the fact that these patients require much more than the normal 10 or 20 per cent increase over basal requirements at rest. As much as 75 or 100 per cent increase over their basals may be necessary to maintain nitrogen equilibrium and bring about a gain in weight in the hyperthyroid patient. From a practical standpoint gain in weight answers the question whether the patient is receiving sufficient food. We have found the B.M.R. a useful guide in securing adequate food intake. It is usually possible by employing concentrated foods to get the patients to take twice as many calories as the B.M.R. calls for.

The role of iodine in the physiology of the thyroid is a fascinating topic but only a few practical phases of the subject can be mentioned. The place this element holds in the prevention of non-toxic hyperplasia of the thyroid gland and its value in preparation of toxic cases for operation is well established. The extent to which iodine reduces the B.M.R. is usually in direct proportion to the initial elevation. In 185 unselected cases we have studied at the Presbyterian Hospital the average drop in the basal after iodine administration when the level was between +20 and +30 per cent was 9 per cent; with an initial basal between +70 and +80 per cent the average drop amounts to between 35 and 40 per cent. The above observation served as a standard with which to compare the effect of diiodotyrosine which has been so enthusiastically recommended in the recent German literature as superior to the inorganic preparation in common use. Chemically diiodotyrosine would seem to be the precursor of thyroxin, moreover almost all of the organic iodine in the thyroid gland is in the form of either thyroxin or diiodotyrosine. On the hypothetical basis that these two organic iodine compounds normally are in equilibrium in the gland, hyperthyroidism might result when thyroxin is present in excess, hypothyroidism when diiodotyrosine predominates. Our chemical studies of normal and pathological glands have failed to bring support to such a hypothesis. The claims made for the therapeutic use of diiodotyrosine is that it reduces experimental hyperthyroidism, known to be unaffected by inorganic iodine compounds; that it is effective in so-called iodine refractory cases; and that iodine escape is less frequent. In a study of thirty cases including three patients who had previously received iodine, we could detect no difference in the effect of diiodotyrosine and that observed with Lugol's solution and sodium iodide. The reducing effect on the basals was commensurate in both preparations, nor was any change produced by diiodotyrosine in the iodine refractory patients. Our clinical experience with diiodotyrosine appears to be consistent with observations made in the laboratory. When rabbits are given gram

doses of diiodotyrosine about 10 per cent is excreted as inorganic iodine, the rest either unchanged or as a lactic acid derivative. When given in the therapeutic amounts of 100 milligram doses to patients a larger percentage may be broken down to give inorganic iodine.

A word of warning against the indiscriminate use of iodine may be ventured. We have already mentioned its use in the adolescent goiter and as a therapeutic aid in selected cases. Long continued use of iodine in patients with nodular glands occasionally transforms a non-toxic gland to a toxic gland. I know of no advantage to be gained in administering iodine to individuals with non-toxic nodular glands. The great value of iodine in bringing about remissions in the toxic glands, either diffuse or nodular, in preparation for operation must always be considered when one contemplates the use of iodine therapeutically in toxic cases. The temporary effect of iodine makes it essential to reserve iodine for pre-operative use. It is true that cases are reported, and I have seen such, demonstrating a control of the toxicity over long periods until spontaneous recovery occurs, but in my experience iodine has proved disappointing in the medical management of toxic goiter. The impression that once the iodine effect is obtained and the patient "escaped", little benefit may be expected in the subsequent use of iodine is not correct. After a period, one to four weeks, without iodine even though it has been administered over a several months' period we note satisfactory responses. It must be said, however, that the second trial often results in a less striking response.

Conclusion

I have endeavored to point out in the foregoing remarks how a knowledge of the deviations from normal of the metabolism in hyper- and hypo-thyroidism may be of service to the clinician. One impression I hope to make. Laboratory tests of function are valuable aids when given their proper place and importance. They have increased

our knowledge of disease and have contributed to our clinical ability. It must be remembered, however, that they often represent single components of a complicated system of dependent variables. The danger not only in diseases of the thyroid, but in Medicine generally, is to become a slave to laboratory data and place too little reliance on good clinical judgment.

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SURGICAL TREATMENT OF HYPERTHYROIDISM*

FRANK H. LAHEY
Boston

It is my desire and purpose to present to you informally the results of our experiences with hyperthyroidism in its typical, in its atypical form and in its association with other diseases.

First I would like to speak about the question of hyperthyroidism in children.

We have seen now a large number of children ranging down to as young as three years of age with typical exophthalmic goitre. At the beginning of our experience with hyperthyroidism, particularly in very young children, we were greatly worried by this condition because of the great capacity of children to react so strikingly to intoxications of any variety. We were impressed, almost intimidated, by the tremendous activation post-operatively and the impressive tachycardias which followed any operative procedures on these cases. This in our early experience with hyperthyroidism in very young children, made us fear to undertake operative procedures on them. With this in mind, we tried first iodine and x-ray on a number of these cases without any satisfactory success and we now wish to make it clear from our experience that hyperthyroidism in children is just the same as hyperthyroidism in adults. We approach it surgically from just the same viewpoint as we do hyperthyroidism in adults. The end results are just as good, the dangers are, however, I think, a little bit greater, and I speak now particularly of the very severe cases.

There are two points which are of practical interest about which we have learned as the result of practical experience in dealing with the surgery of hyperthyroidism in children, and they are: one, that children have such a

* Delivered October 24, 1933.

great capacity for intense toxic reaction post-operatively that we think in the very intensely toxic cases in children, it is always wiser to divide the operation into two stages, doing a right subtotal thyroidectomy first, sending the child home for six weeks, then having them back and doing a left subtotal thyroidectomy. This procedure, as in adults, may be one of hypercaution but certainly, when one deals with a condition such as hyperthyroidism in children in which the mortality rate is a little higher than with adults, it is, I believe, wise to be on the safe side.

The other feature concerning hyperthyroidism in children, particularly young children is the matter of the amount of thyroid tissue to be removed.

In adults, the penalty for removing too much thyroid tissue and producing myxedema is not very great since artificial thyroid feeding is almost a complete and satisfactory substitute for natural thyroid secretion. In children, however, thyroid secretion is not only necessary for the maintenance of metabolism but is also essential for developmental effects. For this reason, the penalty for the production of myxedema in a very young child may very definitely be of more serious consequence than that in adults. With this in mind, we have taken the position that when one does subtotal thyroidectomy in particularly young children, a larger remnant of thyroid than in adults should be left behind to guard against the possibility of the production of myxedema.

I wish now to speak of a typical type of hyperthyroidism which we have for practical purposes, termed "apathetic hyperthyroidism."

There are two types of hyperthyroidism or exophthalmic goitre with one of which everyone is familiar, that is, the typical activated exophthalmic goitre which is so characteristic of the disease, typified by exophthalmos, goitre, tachycardia, tremor, flushed skin, activation, rapid pulse and so forth. No one can mistake the diagnosis in a frank case of activated hyperthyroidism of this type.

We have often said that activated hyperthyroidism of this type when fully developed, can be diagnosed by the merest tyro. Not alone is this true but the condition so flies its own danger signals that one is always impressed with the seriousness of this state.

We have from time to time written, however, of another condition of hyperthyroidism which we have termed "apathetic hyperthyroidism."

There has been some criticism concerning the employment of the term "apathetic hyperthyroidism" and such criticism, I believe, is logical. It has been stated that apathetic hyperthyroidism is no different in origin than activated hyperthyroidism and that it is one and the same disease except that it occurs in the aged and that it has existed usually in a chronic state over a considerable period of time.

The above is true but we have particularly coined the term "apathetic hyperthyroidism" not because we wish to establish any new entity, but because we believe that by marking this group with such a term that so aptly describes it, attention may readily be focused upon it, it may thus be diagnosed more often and earlier and this condition is very frequently overlooked, due to the fact that apathetic hyperthyroidism is so non-obvious in its symptoms. Furthermore, we have particularly desired to call attention to this group under a separate heading, such as apathetic hyperthyroidism, because we feel certain that the operative seriousness of this group is not fully appreciated and if we can call attention to it by describing it by its outstanding feature, apathy, then not only can we perhaps make it easier to diagnose but also be more certain that the seriousness of such states will be appreciated.

Apathetic hyperthyroidism differs from activated hyperthyroidism primarily in the fact that patients with typical hyperthyroidism are agitated and activated while patients with apathetic hyperthyroidism tend to be calm, slow and even, as the term suggests, apathetic. Patients with acti-

vated hyperthyroidism of the typical type tend to have striking eye signs such as stare, diminished frequency of winking and exophthalmos. Patients with apathetic hyperthyroidism tend to have calm eyes with none of these signs. Patients with activated hyperthyroidism tend to have a large, firm thyroid gland. Patients with apathetic hyperthyroidism tend to have firm but small and pebbly thyroid glands. Patients with activated, typical hyperthyroidism tend to have a pounding apex beat, as we have frequently said, diffused over the entire precordia, while patients with apathetic hyperthyroidism tend to have no striking apex beat. The pulse rate in patients with primary hyperthyroidism is high. The character of the pulse is toxic. The pulse rate in apathetic hyperthyroidism is persistently but moderately elevated and is not toxic in character. The skin in the patients with activated hyperthyroidism is hot, soft and flushed. One is particularly apt to be impressed that when an elderly patient has activated hyperthyroidism, she appears much more youthful due to the soft, hot, flushed skin which is associated with activated typical hyperthyroidism. The skin in patients with apathetic hyperthyroidism, however, is cool, pigmented and wrinkled. What the cause of the pigmentation is, we are unable to say but following the relief of hyperthyroidism, this pigmentation usually disappears. The basal metabolism in activated hyperthyroidism tends to be markedly elevated. The basal metabolism in apathetic hyperthyroidism is elevated but only moderately so. One of the outstanding features of apathetic hyperthyroidism is weight loss. Many of the patients with apathetic hyperthyroidism have lost fifty, sixty and even one hundred pounds in weight but over such a number of months or years that the patient is not impressed with the seriousness of it.

When fatalities occur in apathetic hyperthyroidism and activated hyperthyroidism, they are of a distinctly different type. Should a patient with activated hyperthyroidism of the typical exophthalmic goitre type die, he will die in delirium, thrashing about in bed, sweating and with uncountable pulse rates.

Should a patient with apathetic hyperthyroidism die, however, for example, following too much surgery as complete subtotal thyroidectomy, he will frequently go back to bed with a very reasonable pulse rate, one hundred and twenty, of good quality, and not toxic in character, he will become drowsy, apathetic and finally comatose and die peacefully with no evidence of activation whatever.

Patients with activated hyperthyroidism, as has already been stated, impress one as being very serious risks while patients with apathetic hyperthyroidism run frequently excellent pulse rates on the table, only to go back to bed following operation and die very unexpectedly.

So impressed are we with the seriousness of the apathetic hyperthyroidism which so frequently occurs in people of advanced years, that when we are certain that hyperthyroidism is of this type, we unhesitatingly divide the operation of subtotal thyroidectomy into two stages.

One should, I think, be suspicious of apathetic hyperthyroidism in all patients who have a persistent, long standing, unexplained myasthenia. One should be suspicious of apathetic hyperthyroidism in all patients who run moderately but persistently elevated pulse rates which cannot be explained otherwise and one should be suspicious always of apathetic hyperthyroidism in patients who have had marked weight loss over a long period of time which cannot be explained.

What are the end results in subtotal thyroidectomy for patients with apathetic hyperthyroidism as compared with those with activated hyperthyroidism? They are equally as good. The lost weight is regained, myasthenia disappears, the pigmentation disappears from the skin, these patients who appear so elderly due to weight loss and wrinkling of the skin, following their recovery from this type of hyperthyroidism drop a number of years from their facial appearances and appear much younger. The end results in subtotal thyroidectomy in the patients with apathetic hyperthyroidism are just as excellent as in those

with subtotal thyroidectomy for activated hyperthyroidism. The two features with which I wish particularly to impress you are that due to the lack of obvious symptoms they are often not diagnosed and due to their moderate course while on the operating table, their seriousness is often overlooked.

I wish now to say a few words concerning the dangers of exophthalmos in patients with so-called exophthalmic goitre or primary hyperthyroidism and I am prompted to make these remarks because we have seen six eyes lost from a severe degree of exophthalmos in patients of this type.

One should realize that any patient with marked exophthalmos needs only to have an ulcer of the cornea to produce œdema, increased lid pressure and finally slough in the eye which will result in the need for enucleation of the entire eye.

One should realize that the cornea of the eye has no real blood supply and that its nourishment is received largely by osmosis. If one now has extreme exophthalmos resulting in severe pressure from the lid edges, due to the protrusion of the eye, the nourishment of the conjunctiva is interfered with and in addition to that the drying which results from diminished frequency of winking, also predisposes to injury of the cornea in these cases with marked degrees of exophthalmos.

One should realize also in preparing patients with exophthalmic goitre for operation that when preliminary narcosis is given, these patients are half asleep, often not fully conscious of what is going on and that it is easily possible for them to rub the sleeve of their nightgown across their prominent exophthalmic eyes, produce an abrasion of the conjunctiva, ulceration, infection and in this way bring about so much œdema that increased lid pressure produces slough and the final loss of the eyes.

One should realize also that following subtotal thyroidectomy occasionally, exophthalmos which was only mod-

erate previous to operation becomes more and more prominent until it is of the serious type. This type of postoperative exophthalmos is most frequently associated with a minus degree of metabolism and associated postoperative myxedema. Fortunately, it is extremely rare but when it occurs it is a most distressing situation requiring very radical measures to remedy it.

One should, I think, bear in mind that any patient with extreme exophthalmos is a candidate for blindness, that they should be cautioned when out on the street to wear goggles and not to get foreign bodies in their eyes. They should be cautioned, when it is due to exophthalmic goitre, that they should submit to surgery as early as possible in order that regression of the exophthalmos may be brought about as early as possible.

When exophthalmos reaches such a degree of prominence that it endangers the eye itself from lid pressure, one may do two or three things. The lid edges may be sutured together and if they are sutured together, they should be denuded of their epithelium so that they will grow together; otherwise, the stitches employed in suturing them together will very soon cut out.

Doctor Howard Naffziger of the University of California in San Francisco has devised an operation which offers these cases of intractable exophthalmos the only real hope when they have reached extreme degrees. It consists in turning down a frontal flap of bone on either side of the skull, elevating the temporal lobe and unroofing the bony orbital canal. This results in decompression of the orbit, permits the eyes to sink back, relieves lid pressure and saves many of these cases. Dr. Gilbert Horrax in charge of the Neurosurgical Department in the Clinic, has operated on two such cases and has saved the eyes in both cases.

It is very important, I think, for me to call your attention particularly to the dangers of extreme exophthalmos and to the measures which can be utilized in saving the eyes when this intractable exophthalmos occurs.

Another type of hyperthyroidism of which I have frequently spoken and which I wish to discuss with you is the question of acute hyperthyroidism, or what we have termed, thyroid crisis. Everyone dealing with hyperthyroidism should remember that even patients with moderate degrees of thyroid intoxication can very quickly progress into such acute stages of hyperthyroidism that delirium, vomiting and extremely severe intoxication occur with the serious possibility of the development of a fatality.

If one appreciates the symptoms which indicate the onset of a rapidly intensifying degree of hyperthyroidism, measures can be taken to offset the effects of this state and thereby not infrequently patients' lives be saved.

If patients are permitted to progress into the acute stages of severe hyperthyroidism amounting to what we have termed thyroid crisis, then fatalities will occur in a considerable percentage of these cases regardless of what measures are employed to combat these states. We have often stated that the acute crises of hyperthyroidism are much like the critical situations in diabetes. If one appreciates the onset, for instance, of diabetic coma or even hyperinsulinism, measures can promptly be instituted which will prevent patients from progressing into serious states in these conditions. Likewise, if one appreciates, as we have already stated, the indications of intensifying hyperthyroidism which may amount to thyroid crisis, measures likewise can be undertaken which will prevent these patients from progressing into these states from which they cannot be extricated.

One should be suspicious of a possible impending thyroid crisis when there is an unexplained, persistent increase in the pulse rate. When patients with hyperthyroidism have been running pulses of one hundred and twenty and show progressive and persistently elevated rates, one should be suspicious of the approach of a thyroid crisis. When patients whose mental states are perfectly clear, show any mental changes, one should be suspicious that this is an early indication of the delirium associated

with an intensifying hyperthyroidism. One should realize that hyperthyroidism, just as is diabetes, is markedly intensified by a superimposed infection. Given a patient with a moderate degree of hyperthyroidism, any severe infection can so intensify this that the patient may be very rapidly converted from a patient with a moderate degree of thyroid intoxication into one with intense intoxication amounting to a thyroid crisis with delirium, diarrhœa, vomiting and uncountable pulse rate. Likewise, one should remember that hyperthyroidism is a disease of hypercombustion and when patients for instance, are vomiting they are distinctly upon a verge of a thyroid crisis. When they vomit, they are unable to take in fluids, they are unable to take in fuel—two very essential elements in combatting hypercombustion. If they do not have fluid and fuel but hypercombustion continues to go on, a vicious circle is established whereby the hyperthyroidism or intoxication is intensified and the factors, such as loss of fluid and fuel, are exaggerated thus again further intensifying the effects of the hyperthyroidism. One should remember also that diarrhœa accomplishes the same result; with ten to fourteen loose movements a day, the fluid and fuel loss is great, the hyperthyroidism is intensified and the two desirable elements which have to do with combatting hypercombustion, fluids and something to burn, are lost. We feel very strongly, therefore, that when one has a patient with hyperthyroidism and any of these indications of intensifying hyperthyroidism are present, urgent measures should immediately be undertaken to offset them and these measures consist of the introduction of fluids, fuel and iodine.

We have always appreciated that one of the best ways to offset the effects of the excessive hypercombustion associated with thyroid crisis is the introduction of salt solution and glucose intravenously. We used to employ, however, the ordinary method of introducing one thousand cubic centimeters at one sitting, and seventy-five to one hundred and twenty-five grams of glucose in the thousand

cubic centimeters of salt solution. This fluid is undoubtedly utilized very quickly in severe and intense hyperthyroidism and likewise, if it is introduced rapidly, some of the glucose is spilled over in the kidney and lost and the remainder rapidly burned so that there are periods perhaps during the twenty-four hours during which particularly fluid is not available for the patient in excessive stages of hypercombustion. This we have overcome by the employment of an intravenous drip method, utilizing the intravenous needle of Doctor G. A. Hendon of Louisville and setting the drip apparatus so that forty to sixty drops of salt solution containing five per cent glucose solution are delivered into the vein constantly.

We no longer introduce this intravenous needle into the median basilic vein because the arms are moved around so violently by delirious patients, the needle is disturbed, displaced and the introduction of the fluid is interrupted. We introduce the needle now into the long saphenous vein above the ankle, strap the rubber tubing down under the sole of the foot and along out by the great toe, then employ a large amount of slack tubing so that the patient can move his foot around even if delirious and not kink it. We used to employ a thermos bottle to keep the solution warm but patients with hyperthyroidism will heat their solutions sufficiently after they get into the vein and most of them have such degrees of excessive heat production that it is good for them to have moderately cool solutions introduced into their circulation. We have likewise learned that one should not employ ten per cent glucose solution since it tends to thrombose the vein. We have frequently used five hundred and more grams of glucose solution in these cases. These needles run day and night in the same vein for four days on an average without requiring changing. We have had one needle run eleven days the twenty-four hours around, delivering forty to sixty drops per minute without requiring change. This, however, is exceptional.

While fluids and fuel in the form of glucose, are extremely essential in the treatment of acute hyperthy-

roidism, so also is iodine. When we first began to treat these patients in thyroid crisis, we were at a loss how to satisfactorily introduce iodine into the circulation. If they were vomiting or had diarrhœa, it could not be satisfactorily given by mouth and for a while sodium iodide intravenously was suggested as a method of supplying iodine in these cases. We have now learned that one can introduce directly into the salt solution which is given intravenously, fifty minims of Lugol's solution daily with no bad effect. It is thus delivered effectually into the circulation where it is needed and if there be a cardiac complication, digitalis likewise can be added to the salt solution.

I would again like to stress the need of appreciating the onset of increasing thyroid intoxication and the presence of an impending thyroid crisis and also impress upon you the fact that if urgent methods of treatment be undertaken, the majority of these patients cannot only be gotten out of crisis, but can be kept out of crisis, can then be put upon a high carbohydrate diet for two or three weeks and gotten in such good condition that a right subtotal thyroidectomy can be done upon them.

It used to be stated that one should not operate upon patients close to a crisis. It is true that one should not operate upon patients before they are out of a crisis but one should not fail to operate upon patients after they are out of a crisis. If these patients are sent home because one fears to operate upon them close to a crisis, some of them will definitely go back into a crisis again and it will not be possible to extricate them a second time. On the other hand, they are usually such serious risks that it is unwise to undertake subtotal thyroidectomy as close as three weeks to a thyroid crisis. In such cases, we do, as already stated, a right subtotal hemithyroidectomy, send the patient home for six weeks then have them back and do a left subtotal hemithyroidectomy. By this measure the course of the disease is interrupted and we are certain that they will not return again in a crisis.

We have repeatedly written on the subject of the association of hyperthyroidism and heart disease and I think it will be of interest to you in this connection for me to review some of our views with you on this subject. First of all, we have always been interested as to whether or not there was an actual thyroid heart. Doctor L. M. Hurxthal in the Medical Department of the Clinic has repeatedly stated that, based upon our observation of a number of thyroid fatalities post-operative and unoperated, we have never been able to determine that there actually was pathological evidence of a destructive action on the part of thyroid secretion on the heart muscle.

If one assumes that the enlargement of the heart, associated with tachycardia is due to the hyperthyroidism and not to work hypertrophy, then this may be a thyroid heart. If one assumes that auricular fibrillation which is so often associated with hyperthyroidism, is evidence of heart damage, then this likewise, as Dr. Hurxthal has stated, may be evidence of a thyroid heart but as far as actual microscopic evidence of heart damage as the result of prolonged hyperthyroidism goes, we have never been able to determine that such a condition exists; so we have felt that there is no true thyroid heart.

Auricular fibrillation is one of the most constant cardiac abnormalities associated with hyperthyroidism. Over eighty-five per cent of all the patients whom we have seen with hyperthyroidism and cardiac decompensation, have had auricular fibrillation. Auricular fibrillation is a most inefficient cardiac rhythm and when it persists in a heart which is already damaged and which is being overdriven by hyperthyroidism, there must constantly be the danger of cardiac failure.

As regards auricular fibrillation and hyperthyroidism, we know from our experience that after the removal of the hyperthyroidism and the employment of quinidin, eighty-five per cent of these patients can be restored to normal rhythm and will remain in normal rhythm.

Regarding the use of quinidin in auricular fibrillation in patients with hyperthyroidism, we have learned some definite things: One is that one wastes the quinidin effect if it be given before subtotal thyroidectomy. One can, in patients with hyperthyroidism and auricular fibrillation, give quinidin and in some of the cases, restore the rhythm to a normal character but upon doing a subtotal thyroidectomy, there will be such a post-operative reaction that absolute irregularity will again occur and the quinidin effect will thus be lost. For this reason, we have established a rule that quinidin is not to be given until five days post-operatively by which time the patients have passed through any thyroid storm or reaction and then when their rhythm is restored to normal rhythm with quinidin, in eighty-five per cent of the cases it will remain normal.

The association of hyperthyroidism and heart disease and the ability of patients with hyperthyroidism and congestive heart failure to stand surgery is to my mind and always has been a most fascinating subject. We have written a great deal about it. We designated this group of cases as thyrocardiacs. We have operated upon a great many of them and have been deeply interested in this field.

I have thought a great deal about this field and often have wondered why patients with such serious cardiac decompensation could withstand surgery as well as they have with such a low mortality rate. We have now operated on three hundred and twelve of these thyrocardiacs with a mortality of only four and six-tenths per cent, not a serious death rate in view of the severity and seriousness of this condition.

The reason that these patients stand surgery as well as they do is not apparent on the surface. It is due to the fact that they are automatically segregated into those who will stand surgery and those who will not before they come to us for consideration. When a patient has very little cardiac reserve and hyperthyroidism is superimposed upon this excessive degree of cardiac damage, he dies and

does not get to us for consideration as to the question of thyroid surgery. When, on the other hand, he is able to get to us or even to live long enough so that his physician and he consider the question of thyroid surgery, he or she of necessity must have a considerable cardiac reserve; otherwise, the burden of the superimposed hyperthyroidism would bring about such cardiac disability that the question of operation could not even be considered. When patients have sufficient cardiac reserve so that the question of operation can be considered, then it is of such an amount that when the hyperthyroidism is removed, they have a surprising capacity for activity.

We have recently reported our end result studies in two hundred and fifty-six of these cases followed from one to ten years. Of that number with hyperthyroidism and cardiac decompensation, over ninety per cent have regained their compensation and retained their compensation so that they are able to be up and about and active. Of all the two hundred and fifty-six cases whom we have been able to find and follow over this period of one to ten years, complete disability now exists only in three cases.

This too is explained by the fact that when patients do not have considerable cardiac reserve, there is not the question of disability but a fatality results.

One can, therefore, say regarding the cases of hyperthyroidism and cardiac complications that the most common cardiac complication is auricular fibrillation, that over eighty-five per cent of these cases following surgical removal of their hyperthyroidism and the employment of quinidin can be restored to normal rhythm, that in a follow-up study of two hundred and fifty-six cases of cardiac decompensation and hyperthyroidism, over ninety per cent have had their compensation restored and their hearts have remained competent over a period of from one to ten years following subtotal thyroidectomy and this with a respectable mortality rate of four and six-tenths per cent.

I wish now to speak of another common complication with which, due to our association with Dr. Joslin in the New England Deaconess Hospital, we have had experience in a number of such cases and that is the association of hyperthyroidism with diabetes. Hyperthyroidism superimposed upon a patient with diabetes is a very undesirable complication since it interferes definitely with the management of his case, it diminishes his tolerance for carbohydrates, increases his demand for insulin and makes the dietary management of his case, due to hypercombustion, difficult.

We have learned that the mortality of the surgery of hyperthyroidism when associated with diabetes is a little bit higher than in a patient who does not have diabetes but being between three and four per cent is within reasonable limits.

We have learned in connection with these cases that there is an increased incidence of glycosuria in patients with hyperthyroidism and that following the relief of hyperthyroidism, this glycosuria disappears. We have likewise learned that the removal of hyperthyroidism in no case has resulted in a cure of the diabetes. One can say as the result of an experience now amounting to well over a hundred and seventy-five cases of hyperthyroidism associated with diabetes that there will be a definite increase in carbohydrate tolerance, that there will be a definite diminution in the need for insulin and that the management of the diabetes will be very much less difficult.

Patients with diabetes and hyperthyroidism should be submitted to surgery not only because of the dangers of the hyperthyroidism but because of the added difficulty in managing the diabetes.

One should have in mind that with the added mortality in this complication, more two stage operations should be done in patients with hyperthyroidism and diabetes than in those with hyperthyroidism alone.

Finally, the last subject of which I wish to speak in connection with hyperthyroidism is that of the association of hyperthyroidism and pregnancy.

It used to be said by the obstetricians that when a patient had hyperthyroidism and pregnancy, the uterus should be emptied. That is not our present feeling. We know that if patients who are pregnant and have hyperthyroidism are permitted to go into the last stages of pregnancy, very serious complications may arise.

We know that if patients with hyperthyroidism have to be given general anesthetics and have major surgical operations performed, in many of the cases as the result of operative trauma and post-operative reaction the hyperthyroidism may be so intensified that a fatality from the hyperthyroidism results. If, then for example, a patient be permitted to go into the late stages of pregnancy and Cesarean section or prolonged labor, requiring instrumental delivery becomes necessary, a fatality as the result of the intensified hyperthyroidism may eventuate.

Our attitude today in the treatment of patients with hyperthyroidism and pregnancy is that they should be submitted to subtotal thyroidectomy at the earliest possible date in their pregnancy. This then relieves them of the hyperthyroidism and if difficulties arise at the time of their labor, there is not the danger then of the establishment of acute thyroid intoxication and a fatality.

We have operated upon nineteen patients in pregnancy with hyperthyroidism. There have been no fatalities in the nineteen cases. One miscarried ten days after operation after driving two hundred miles home from the hospital. This hardly can be attributed to the operation and I do not believe that there is any particular danger of difficulty with the baby in relation to the operation of subtotal thyroidectomy for hyperthyroidism in pregnancy. We, therefore, strongly urge that when patients who are pregnant have hyperthyroidism, the diagnosis be made and the operation be performed at the earliest possible date in their pregnancy.

I have tried to present to you the various aspects of hyperthyroidism from the practical point of view from our own experience with the condition and I think perhaps you would be interested in what the mortality rate has been in the Clinic dealing with these cases.

We have now done something over twelve thousand thyroid operations. The mortality rate in exophthalmic goitre has ranged from eight-tenths of one per cent down to one-tenth of one per cent last year. Last year was our most successful year because we operated upon one thousand and twenty-one goitres with but one death. One should recall, however, that the mortality of toxic adenoma will always be higher than the mortality of primary hyperthyroidism, one and eight-tenths per cent in our experience, due to the greater age of these patients. The mortality in adenoma and the various other thyroid states is almost of trivial amount.

One should also remember that the mortality rate in thyroid surgery will never be the same as the mortality rate in hernia, fibroid operations, appendicitis and various other general surgical conditions. Thyroid surgery is not a type of surgery which can be done casually. When it is done casually the mortality will be prohibitively high. When, on the other hand, it is done by organized groups with good medical preparation, with good technical operative assistants, with good anesthesia and with good post-operative care, the mortality will be low and the eventual results as satisfactory as following any operation in surgery.

MINERAL METABOLISM*

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In no constituents of the body is the so-called "homeostasis" of Cannon more strikingly maintained than in the inorganic salts. These salts are composed of a number of bases and a number of acid radicles, which respond in an accurate, coordinated way so that they balance each other, not only to maintain the pH of the body but also to help maintain the constant osmotic pressure of tissue fluids. In the body, because of the great efficiency of the normal kidney, an excessive intake of either acid or base can be readily eliminated. By such means as this the body cells are bathed by a solution which remains extraordinarily constant in salt content. Probably the content of no substance remains so constant in the body tissues as do the inorganic bases. Normally at the level of 150-160 milliequivalents it varies only very rarely as much as 10 milliequivalents from the normal. It is obviously of enormous importance to keep the bases in the blood at a constant level, a level which is not far removed from the concentration of base in sea water at the time when we are supposed to have emerged from it. In order to maintain this constant level it is essential that water and salts should fluctuate together, so the generalization can be made that in disease, when excess base is lost by excretion, water is also lost and dehydration follows; when base is retained, so also is water, and edema results.

One of the striking and unexplained phenomena of the salts in the body is the distribution of base. Sodium is the predominating base of all the fluids outside of the cells, while potassium predominates inside all of the cells. As a result, when fluids are lost from the body it is largely

* Delivered October 25, 1933.

sodium salts which are excreted. This is well illustrated by the fluid losses in burns, diarrhoea, or excessive vomiting. Here the body becomes depleted of its sodium salts so that they must be replenished.

On the contrary, when body cells are broken down there is a depletion of potassium salts. This may be seen in starvation, where breakdown of tissue is associated with a mounting elimination of potassium through the kidney. At the same time, the excretion of sodium from extra-

TABLE I.

URINARY EXCRETION DURING FASTING*

Days of Fast	Calcium gms.	Potassium gms.	Sodium gms.
2-4	.24	1.37	.93
5-6	.27	1.45	.28
10-11	.22	1.01	.10
18-19	.25	.68	.05
24-25	.17	.79	.06
30-31	.14	.61	.05

cellular fluids falls to a very low level so that the total base content of the blood plasma remains constant (Gamble, Ross, and Tisdall[1]) even after a prolonged fast. Remembering that it is essential to health to maintain the normal salt concentration in the body, as well as to maintain a normal volume of blood, let us see what happens superficially in two diseases in which these levels are sorely strained, namely, intestinal obstruction and nephritis.

The work of Gamble and McIver[2] has taught us much in regard to the effects of intestinal obstruction. The gastric juice contains not only a large amount of hydrochloric acid but also a considerable amount of sodium. Bile and pancreatic juice also have as much sodium in them as has the blood serum and they are alkaline in reaction. This large amount of base and of chlorine ions, which is poured into the intestinal tract, is reabsorbed in health, but in certain clinical conditions they may be lost. Thus, ex-

*Taken from Benedict, F. G., A Study of Prolonged Fasting, Carnegie Institution of Washington, 1915.

cessive vomiting with or without intestinal obstruction, or bile fistulae, or even severe diarrhoeas are all associated with a loss of base and of chlorine. The importance of these secretions in regard to fluid as well as salts is well illustrated in the work of Rowntree.

TABLE II.

AN ESTIMATE OF THE RELATIVE DAILY VALUES OF SECRETIONS POURED INTO THE INTESTINAL TRACT OF MAN*

	cc.
Saliva	1500
Gastric juice	2500
Bile	400
Pancreatic juice	600
Succus entericus	3000
	8000
Total blood plasma	3500

* Taken from Rowntree, L. G., *Physiol. Reviews*, 1922, II, 116.

It is dramatically evident, when one compares the total volume of blood plasma to the daily volume of intestinal secretions that a precarious situation may result from the loss to the body of these secretions. If the vomiting is gastric, there is more chlorine lost than base, if it involves the bile and pancreatic secretion there is apt to be an excess of base lost in the fluid.

So as not to complicate the problem too much, let us consider pyloric obstruction alone, which has been well studied by Gamble[2]. The loss in this condition is largely hydrochloric acid and sodium. This loss may be great and is complicated by the obvious inability of the body to replace this loss by eating. There follows a greater loss of chlorine than of sodium. As a result, there is a tendency to an alkalosis with the resulting picture of "gastric tetany." Chlorides in the blood may fall to less than half the normal concentration (McVicar, C. S.[3]), a loss which is far greater than that of base. The body can stand this disproportionate loss very poorly and, therefore, gets back to a relative balance by excreting more base by urine. The result is a very marked fall in base as well as chlorides

in the plasma. This condition demonstrates dramatically how essential are inorganic salts to health, for there is a rapid appearance of the picture of intense dehydration, diminished urinary output, nitrogen retention, with an eventual collapse and death. The treatment for it is simple and is the same for all of the diseases in which excessive intestinal contents are lost: sodium chloride and water in adequate amounts. By adequate amounts is meant enough to cause a good flow of urine so that any excess of chlorides or of base are separately dealt with by the kidneys. No other treatment seems an adequate substitute. Water alone, or soda bicarbonate alone, or glucose (Walters, W. and Bollman, J. L.[4]) or ammonium chloride are not satisfactory (Gamble, J. L. and Ross, L. G.[5]), for all three of the essential substances which have been lost must be replaced, and water, sodium, and chloride must be given. With adequate kidneys, a fairly rapid adjustment is made and the components which are given in excess are excreted while those sorely needed by the body are retained. A similar situation has recently been demonstrated in Addison's disease (Harrop[6]).

The lavish loss of water and sodium and chloride, which may result from intestinal abnormalities, is in great contrast to the work of the kidneys. In the secretion of urine by normal kidneys, each inorganic component of the plasma is excreted only when present in excess. As a result, the normal kidney maintains a quite constant environment for the body cells, as long as the various constituents are adequately supplied. With kidney damage, however, the accuracy of the mechanism may be lost and salts and water may be retained or excreted in excess. This is soon followed by symptoms.

In the edema of nephrosis, the reduction of the plasma proteins plays a most important part which cannot be discussed this evening. However, the inorganic salts are also seriously involved for where there is edema there is retention not only of water but also of sodium and chloride. We

speak clinically of chloride retention, meaning retention of inorganic salts. This term is used because of the fact that the chemical analysis for chlorides is simpler than that for base. It is probable that sodium has far more to do with edema than has chloride retention. Good evidence for this lies in the tendency to retain water when sodium bicarbonate is given and to produce diuresis when ammonium chloride is administered. All of the retained salts and water stay in the tissues, for Van Slyke[7] has shown that the volume of blood plasma in edematous patients is quite normal, while Peters has shown that the total base in the blood plasma is usually lower than normal (Peters, J. P., Wakeman, A. M., Eisenman, A. J., and Lee, C.[8]).

The retention of sodium, chloride, and water is not the invariable result of kidney damage. In fact, in the advanced stages of nephritis, where large quantities of dilute urine are excreted, sodium and chloride may be washed from the body. Under such conditions, Peters[8] has found that the total content, as well as concentration, of sodium salts in the body may be definitely reduced and with this, of course, is associated dehydration.

From the point of view of these findings, it becomes obvious that the treatment of nephritis will vary according to the condition of the body fluids. In patients with edema and stored sodium chloride, salt intake should obviously be restricted, but in nephritics where dehydration from polyuria is marked the ingestion of adequate salt is indicated and needed.

What has been said, in both of the abnormalities discussed, suffices to bring out the fact that the primary inorganic salt involvement in volume changes of extracellular fluid has to do with abnormalities of sodium and of chloride. In changes which involve body cells, however, as in starvation, the important loss from the body is the predominating base of tissue cells, potassium.

So far, this discussion has referred to the salts of the soft body tissues. These salts exist only in the necessary concentration in the active protoplasm of cells and the fluid which bathes them. There is no large storehouse of these salts. If they are lost from the body the sole source of replenishment is from food or medication. However, there is one large storehouse for inorganic salts from which, in time of need, large quantities of base and acid can be drawn. The bones, in this regard, resemble the fat storehouses in the caloric requirements of the organism. The role of calcium and of phosphorus is, therefore, of interest in two ways: first, in their deposit in the bones and, secondly, in the liberation from the bones to satisfy the needs of the organism as a whole.

In the metabolism of bone we clinicians are apt to speak too simply of calcium metabolism. It must be remembered that phosphates are fully as important as is calcium. This is quite well recognized now in rickets where an inadequate phosphate intake may be of prime importance. An excellent example of this is found in the work of Theiler[9]. He studied the disease of Lambsiekte in cattle on the South African veldt. These herbivorous animals had the extraordinary habit of eating the bones of dead animals of their own kind. Theiler found that this proved lethal because of a botulinus infection which was spread by this osteophagia. Why should herbivorous animals eat bones? This he found was due to a deficiency of phosphorus in the grasses used for grazing, and, by making adequate amounts of inorganic phosphates available to the cattle, he promptly caused osteophagia to cease. This discovery was of great economic, as well as scientific value. It serves as an excellent example of the need of the body for phosphates, a radicle equally as important as calcium, to which it is so closely related.

Calcium and phosphorus metabolism differ from the other inorganic salts because they are continuously going in and out of the bones, and are continuously being excreted, even in starvation. If the normal level of calcium

in the blood is changed, effects are seen in muscle tone. A low blood calcium, below 7 mg. per cent, is associated with an increased neuromuscular irritability, or tetany. A high blood calcium leads to low muscle tone, an increased calcium excretion, and abnormal changes in the bones and kidneys.

The maintenance of this normal calcium level is more complicated than that for sodium, for several factors other than the kidney affect it. First, there must be adequate absorption of calcium. This is obviously difficult and in certain diseases like steatorrhoea or Gee's disease it cannot be adequately accomplished. In this digestive disease there is difficulty in absorbing fats and soaps, resulting in the excretion of insoluble calcium soaps in the bulky diarrhoea, thus preventing the absorption of calcium into the body. The result is a gradual thinning of the bones with the development of osteomalacia, and an eventual fall of the blood calcium and tetany. Vitamin D improves the absorption of calcium from the intestine and in very large quantities will relieve this condition.

Except for this effect of Vitamin D, little is known of the factors which influence the absorption of calcium. Once absorbed, calcium may either be deposited in the bones or excreted. The retention in the bones may be large, certainly as much as a gram a day for short periods. This storehouse, however, is not an inert deposit, for the bones are continuously giving up and replacing their salts, and there is good evidence that calcium probably leaves one part of the bones to be redeposited in other parts. How this calcium is deposited and liberated is not always clear. Certainly, there are cells—the osteoblasts, associated with new bone formation; and the osteoclasts, associated with the absorption of bone tissue. Osteoclasts are described in bone which is being depleted by parathyroid hormone[10], and in hyperthyroidism[11]. It is not known whether bone salts can be absorbed or deposited without the presence of these cells. It is hard to believe that the ingestion of acid salts, which increase calcium excretion, causes this

liberation from bones by the activity of osteoclasts, but this problem is not yet settled. At any rate, bone salts are easily pulled from or deposited in the bones. The chief seat of this calcium storehouse is in the bone trabeculae near the epiphyses. These trabeculae can easily be depleted by a low calcium diet and can be replaced by increasing the calcium intake. The bone shafts are less seriously involved, though recent work has indicated that they may also show microscopic evidence of absorption in hyperparathyroidism and hyperthyroidism[10, 11].

What are the known factors which influence this store and influence the level of calcium in the blood? They include internal secretions, vitamins, and foods.

The parathyroid glands are probably the most important of these factors in the normal regulation of the body calcium. Their primary influence seems to be upon the level of blood calcium and phosphorus. From a normal level of 10 mg. per cent, the calcium falls after parathyroid extirpation to 4 or 5 mg. per cent. Signs of intense tetany develop in about twenty hours, when the blood calcium has fallen below 7 mg. per cent.

The lowered serum calcium causes intense irritability of the neuromuscular mechanism and the laryngeal and muscular spasms and generalized convulsions are evidence of this. Calcium excretion on a low calcium intake falls to a minimum. When parathormone, the active principle of the parathyroid gland, is injected intramuscularly there is a latent period of four hours, after which the blood calcium rises and tetany disappears for approximately twenty hours.

If an overdose of parathormone is given, or with an overacting parathyroid adenoma, the blood calcium rises above normal and may even reach 20 mg. per cent. This condition of hyperparathyroidism is being described to you later by Dr. Jaffe. Here, therefore, it need only be said that the amount of calcium absorbed from the intestines is not influenced by parathormone and that the increased

calcium in the blood and urine, resulting from overdoses of the hormone, comes from the bones. This is evident from the experimental work of Jaffe and Bodansky[10], which showed bone changes even with probably adequate calcium in the food. With very high calcium diets, however, these cases can be maintained in calcium equilibrium[12] or even a positive balance. What the bones would then show I do not know. It is interesting that an immunity develops towards commercial parathormone, prepared from cattle, so that after several weeks or months of use the blood calcium sinks back to its original level. This must be an immunity to a foreign protein, for no such immunity follows the oversecretion of a parathyroid tumor. One such case, of twelve years' duration, is known to have maintained a high blood calcium for the last seven years of the disease.

The action of parathormone is mimicked in every way by large doses of Vitamin D. This was first pointed out, I think, by Porges[13], who cured a chronic case of tetany by means of viosterol. Taylor, Weld, Branion, and Kay[14] also showed this close relationship and recently Kozelka, Hart and Bohstedt[15] have shown that parathyroidectomized puppies can reach maturity and can raise normal offspring by the use of large doses of viosterol. The differences seem to be that viosterol aids in the absorption of calcium from the intestine, and its effect lasts for days, while parathormone lasts for only a matter of hours. It is important to remember that a high blood calcium level is nearly always due to overactivity of the parathyroid glands or to overdosage with vitamin D. I think there is also a very rare case associated with an excess of protein in the blood. A low blood calcium level means parathyroid or vitamin D deficiency, or a deficient calcium absorption. Calcium is also somewhat reduced when plasma proteins are low (Peters). Although the parathyroids and vitamin D are the factors which affect *blood* levels of calcium, they are not the only influences which affect calcium metabolism. Abnormal calcium *excretion* can be stimulated by other

means. The thyroid hormone is an important influence, since oversecretion of the thyroid gland increases the excretion of calcium enormously, while in myxedema the demands upon calcium stores are markedly reduced[16]. The thyroid secretion exerts no effect upon the normal level of blood calcium. Its action rather seems to stimulate the catabolism of bone, which results in excessive excretion.

An acid diet is the last factor I want to speak of, for a large excess of acid can increase the excretion of calcium approximately as does parathormone, but this factor again does not appreciably affect levels in the blood[17].

Table III shows the various laboratory combinations which are important in diagnosis.

TABLE III.

ANALYTICAL FINDINGS IN VARIOUS TETANIES AND RELATED DISORDERS

DISEASES	BLOOD PLASMA VALUES				EXCRETION DURING LOW CALCIUM DIET			
	Calcium	Phosphorus	pH	Phosphatase*	Urine Ca	Urine P	Feces Ca	Feces P
Tetany due to Parathyroid deficiency	low	high	normal		low	low	normal	normal
Hyperparathyroidism	high	low	normal	high	high	high	normal	normal
Steatorrhea—Difficulty in absorbing calcium from the intestines	normal or low	low	normal	normal or slightly high	low	high	high	normal
Osteomalacia from Deficiencies and Rachitis	normal or low	low	normal	high	low	low	low	low
Hyperthyroidism	normal	normal	normal	high	very high	very high	high	high
Paget's Disease (Osteitis Deformans)	normal	normal	normal	very high	No marked variation			
Gastric Tetany	normal	normal	increased					

* See Kay, Physiological Reviews.

From these factors the treatment of low calcium tetany is clear.

1. A high calcium diet, possibly with added acid salts like ammonium chloride.
2. Intravenous or intramuscular use of calcium gluconate for immediate effect. For more lasting effects which, however, are not obtained for some hours, one should employ No. 3.
3. Large doses of viosterol to raise the blood calcium level. Because no immunity develops to this, it is preferable to No. 4.
4. Parathormone.
5. Thyroid medication, which is well worth remembering.

To practitioners of medicine, I cannot abstain from mentioning the importance of calcium during pregnancy. It has been shown by Schmidt[18] and others that an enormous amount of calcium can be stored in the bones during pregnancy. That it is important to accomplish this by a high calcium diet throughout pregnancy is self evident, when one realizes that a negative calcium balance can probably not be avoided throughout the period of lactation. Further evidence of strain upon the calcium metabolism is indicated by the interesting work of Kozelka, Hart, and Bohstedt[15]. Their parathyroidectomized dogs could be maintained with a normal blood calcium by daily doses of 14 rat units of vitamin D. During pregnancy, however, 4,000 to 26,000 were required and during lactation as many as 66,000 rat units were necessary. This extraordinary demand implies some mechanism which we do not yet understand.

It is also important to realize that several heavy metals behave in the body approximately as does calcium. Lead[19], mercury[20], and radium[21] are influenced by the same procedures that influence calcium. They are stored in the bones and are liberated from this storehouse in increased amounts when calcium is liberated. This offers a method

of treatment which allows the most readily available of these metals to be pulled from the bones and excreted[19]. The remainder is excreted very slowly, just as is calcium.

What is the interrelationship in body fluids of these ions which are stored, such as calcium and phosphates, to those which have no storehouse, like sodium and chloride? In the first place, the concentration of the calcium and phosphorus is relatively very small. Variations which double their concentration would not affect the total level of acid or base in the plasma more than occurs physiologically, and there does not appear to be much readjustment in other ions to such a change. These ions with low concentration in body fluids, may therefore cause dramatic signs and symptoms quite independently of other ions. Total base or chloride excretion is not influenced by the giving of parathormone, which dramatically increases the calcium and phosphorus elimination[22]. Thus, there is a good deal of independence of excretion of each of these substances and yet they remain closely related as a whole, keeping an accurate balance between acids and bases to maintain the normal pH of the body, and keeping normal the osmotic pressure and the inorganic salt environment—a group of substances which maintain a remarkable equilibrium in spite of the possibility of individual divergence from the norm.

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PROCEEDINGS OF ACADEMY MEETINGS

JANUARY

ANNUAL MEETING—January 4

I. Executive Session—Reading of the Minutes; Election of Fellows and Members; Presentation of Diplomas; Announcement re: Amendments to By-Laws introduced at the Stated Meeting of December 7, 1933.

II. Presentation of Annual Reports—(Read by title) The Council, The Trustees, The Treasurer, Committees.

III. Addresses of the Evening—a. Activities of the past year, Bernard Sachs; b. Presentation of Thomas W. Salmon Memorial Committee Report and portrait of Dr. Salmon, C. C. Burlingame; c. *Symposium on Encephalitis* with especial reference to the St. Louis outbreak; 1. Clinical and research aspects of the St. Louis epidemic, Ralph S. Muckenfuss, St. Louis; 2. Epidemiology, James P. Leake, Washington; 3. Recent research in the disease, Leslie T. Webster; 4. Clinical observations, Josephine B. Neal; 5. The importance of differential diagnosis, Frederick Tilney; 6. Discussion and summary, Thomas M. Rivers.

THE HARVEY SOCIETY (IN AFFILIATION WITH THE ACADEMY)—January 18

THE FOURTH HARVEY LECTURE, "The Estrogenic Substances," E. A. Doisy, Professor of Biological Chemistry, St. Louis School of Medicine.

SECTION MEETINGS

SECTION OF DERMATOLOGY AND SYPHILOLOGY—January 2

I. PRESENTATION OF CASES FROM a. The Polyclinic Hospital; b. The Good Samaritan Dispensary.

SECTION OF SURGERY—January 5

I. PRESENTATION OF CASES—a. A new instrument for intestinal anastomosis, Henry Dawson Furniss; b. 1. Raynaud's Disease—brachial periarterial sympathectomy without relief; 2. Raynaud's Disease—inferior cervical and second dorsal sympathetic ganglionectomy; 3. Thrombo-angiitis obliterans—peripheral nerve alcohol injection for relief of pain, Beverly Chew Smith; c. Three cases illustrating paper of the evening, Norman F. Laskey (by invitation).

II. PAPERS OF THE EVENING—a. The relief of pain in thrombo-angiitis obliterans by peripheral nerve section, Norman F. Laskey (by invitation), Samuel Silbert; b. Delayed and non-union of fractures in the light of aseptic bone necrosis, Eugene J. Bozsan.

III. GENERAL DISCUSSION—Howard Lilienthal, Samuel Silbert, Frederic W. Bancroft, Edwin A. Spies.

JOINT MEETING—SECTION OF NEUROLOGY AND PSYCHIATRY and the NEW YORK NEUROLOGICAL SOCIETY—January 9

I. PAPERS OF THE EVENING—a. Clinical manifestations of female sexual deviations, Adolph Stern; b. The question of psychic suicide, A. A. Brill; c. Concepts and misconcepts about the principles of the psychoanalytic method, Karen Horney, Chicago (by invitation).

II. DISCUSSION—Louis Casamajor, Monroe A. Meyer, Gerald R. Jameison, Marion E. Kenworthy, Sandor Rado (by invitation).

SECTION OF HISTORICAL AND CULTURAL MEDICINE—January 10

I. PAPERS OF THE EVENING—a. Humorous sidelights in early prints on arthritis and gout (with lantern slides), Reginald Burbank; b. Charles Darwin (1758-1778), Withering and the introduction of digitalis, John F. Fulton, Yale University School of Medicine (by invitation).

II. GENERAL DISCUSSION.

SECTION OF PEDIATRICS—January 11

Papers by members of the Department of Pediatrics, New York University, and from Children's Medical Service, Bellevue Hospital.

I. DEMONSTRATION—Exhibit of enlarged colored transparencies of lung sections showing various forms of pneumonia, Charles Hendee Smith, Irving Graef, Elizabeth T. Andrews.

II. PAPERS OF THE EVENING—a. Anaphylactogenic properties of raw, heated, acidified and dried milks, Bret Ratner, Miss Helen L. Gruehl; b. Hematogenous dissemination in tuberculosis of childhood, Edith M. Lincoln; c. Paracentesis of the pericardium as a therapeutic procedure, Lucy Porter Sutton; d. Serum treatment of pneumonia in childhood, Rosa Lee Nemir.

SECTION OF OPHTHALMOLOGY—January 15

I. INSTRUCTION HOUR, 7 to 8 o'clock—External diseases, symptomology, pathology and treatment, Algernon B. Reese.

II. DEMONSTRATION HOUR, 7:30 to 8:30 o'clock—a. Slit lamp studies, Milton L. Berliner, Isadore Goldstein, Wendell L. Hughes, Girolamo Bonaccolto (by invitation); b. Stereoscopic pictures of corneal lesions, Wendell L. Hughes, L. D. Redway (by invitation); c. Case examinations.

III. SECTION MEETING, 8:30 to 10:30 o'clock—a. Reading of the minutes; b. Case reports: 1. Vernal catarrh—its surgical treatment—2 cases, Isadore Goldstein; 2. Retinoblastoma, M. Jaffe (by invitation); 3. Metastatic carcinoma of the retina, Sigmund A. Agatston; 4. Excision of staphyloma of cornea, Daniel B. Kirby; c. Scientific papers: 1. Corneal transplantation with case presentations and moving picture of operative technique, Ramon Castroviejo (by invitation); 2. Microscopic pathology of a case of corneal transplantation, Bernard Samuels.

JOINT MEETING—SECTION OF MEDICINE AND SECTION OF DERMATOLOGY AND SYPHILOLOGY—January 16

I. PAPERS OF THE EVENING—Erythema multiforme dermatoses as related to systemic disease; a. Dermatological aspects, Lloyd W. Ketron, Johns Hopkins University (by invitation); b. Medical aspects, Asa Liggett Lincoln.

II. GENERAL DISCUSSION—Wendell J. Stainsby, E. W. Abramowitz, George Clinton Andrews.

SECTION OF OTOLARYNGOLOGY—January 17

I. PAPERS OF THE EVENING—*Symposium*: *How to obviate failures in the results of surgery in otolaryngology*: a. in tonsillectomy, David H. Jones; b. In paranasal sinus surgery, Robert E. Buckley; c. In simple mastoidectomy, Marvin F. Jones; d. In radical mastoidectomy, John R. Page; e. In blood vessel surgery, Duncan Macpherson; f. In brain surgery, Leo M. Davidoff. Discussion opened by John D. Kernan, C. J. Imperatori, Wesley C. Bowers, William H. Turnley (by invitation).

II. GENERAL DISCUSSION.

JOINT MEETING—SECTION OF GENITO-URINARY SURGERY and the NEW YORK SOCIETY OF THE AMERICAN UROLOGICAL ASSOCIATION—January 17

I. PAPER OF THE EVENING—Clinical evaluation of dye therapy in urinary infections, H. W. E. Walther, New Orleans (by invitation). Discussion: Julius J. Valentine, Oswald S. Lowsley, Abraham L. Wolbarst (by invitation).

II. GENERAL DISCUSSION.

SECTION OF ORTHOPEDIC SURGERY—January 19

I. PRESENTATION OF CASES—a. Tuberculosis of the long bones—three cases, Raymond W. Lewis; b. Tuberculosis of the ankle and knee joint treated by fusion—two cases, L. A. Lantzounis (by invitation); c. Tuberculosis of the spine and hip treated by fusion—two cases, George Inge (by invitation).

II. PAPERS OF THE EVENING—a. Conservative treatment of joint tuberculosis, Horace LoGrasso, Perrysburg (by invitation); b. Surgical treatment of joint tuberculosis, Mather Cleveland.

III. DISCUSSION—Benjamin P. Farrell, Samuel Kleinberg, Brainerd H. Whitbeck (by invitation), Philip W. Nathan.

SECTION OF OBSTETRICS AND GYNECOLOGY—January 23

Program arranged by the Gynecological Staff of the New York Post-Graduate Hospital.

I. PRESENTATION OF CASES—a. Krukenberg tumor of the ovary, Salvatore di Palma. Discussion to be opened by Thomas A. Gonzales. b. Intravesical repair of vesico-vaginal fistula, Thomas H. Cherry. Discussion to be opened by Henry C. Falk.

II. PAPERS OF THE EVENING—a. Primary sterility relieved by conization of the cervix (preliminary report), Robert B. Walker (by invitation). Discussion to be opened by I. C. Rubin. b. A contribution to the treatment of trichomonas vaginalis vaginitis, I. W. Kahn. Discussion to be opened by Francis Sovak. c. Sterilization of the female by coagulation of the uterine cornu (preliminary report), Mortimer N. Hyams. Discussion to be opened by A. H. Aldridge. d. The factors involved in torsion of ovarian neoplasms, Gerard A. Moench. Discussion to be opened by Howard C. Taylor, Jr.

III. GENERAL DISCUSSION.

NEW YORK MEETING OF THE SOCIETY FOR EXPERIMENTAL BIOLOGY AND MEDICINE UNDER THE AUSPICES OF THE NEW YORK ACADEMY OF MEDICINE—January 17

I. Estimation of anterior pituitary-like hormone in cord blood, S. H. Geist, F. Spielman.

II. Absence of effect of antuitrin-S injections on the immature ovary, S. H. Geist.

III. Presence of oxytocic substances in urine during labor, J. R. Cockrill, E. G. Miller, Jr., R. Kurzrok.

IV. Local organ hypersensitiveness. VII. Demonstration of agglutinins in tissues of the rabbit eye following immunization with *Eb. typhi* vaccine, B. C. Seegal, D. Seegal.

V. Passage of native proteins through the normal gastro-enteric wall, B. Ratner, H. L. Gruehl.

VI. A method of obtaining undiluted tissue juice for the study of tissue antibody titer, B. C. Seegal, D. Khorazo.

VII. Serological distinctions between the viruses of encephalitis in St. Louis, 1933, equine encephalomyelitis, and vesicular stomatitis, H. R. Cox, G. L. Fite, Introduced by L. T. Webster.

VIII. Antigenic action of the specific polysaccharide of pneumococcus type I in man, T. Francis, Jr., Introduced by O. T. Avery.

IX. An internal electrocardiographic lead, A. Lieberson, F. Liberson, Introduced by N. F. Blau.

NEW YORK PATHOLOGICAL SOCIETY—January 25

I. DEMONSTRATION OF PATHOLOGICAL SPECIMENS.

II. PAPERS OF THE EVENING—a. Congenital nephritis, Chester R. Brown; b. Widespread amyloid degeneration with occult multiple myeloma, Sheldon A. Jacobson, Theodore T. Fox (by invitation); c. The normal anatomical structure of the calvarium in various age groups, Sidney A. Bernstein (by invitation); d. Rheumatic fever and periarteritis nodosa, Charles K. Friedberg (by invitation), Louis Gross.

RECENT ACCESSIONS TO THE LIBRARY

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Pribram, E. Klassifikation der Schizomyceten.
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Robinson, W. J. The treatment of gonorrhea. 4. ed.
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Sellew, G. Pediatric nursing. 3. ed.
Phil., Saunders, 1934, 609 p.

Willis, R. A. The spread of tumours in the human body.
London, Churchill, 1934, 540 p.

FELLOWS AND MEMBERS ELECTED JANUARY 4, 1934

For Fellowship:

Aaron E. Parsonnet ..... 3 Madison Avenue, Newark
Gaetano J. Mecca ..... 117 West 13 Street
Samuel Maurice Kaufman ..... 321 East 17 Street
Maurice Goldberg ..... 1070 Park Avenue

For Membership:

Samuel H. Averbuck ..... 57 East 88 Street
Gerald Frank Machacek ..... 32-29—38 Street, L. I. C.
Edgar Erskine Hume ..... Army Medical Library, Washington
Charles St. John Butler ..... U. S. Naval Hospital, Brooklyn
William Vernon Cone ..... 687 Pine Avenue, W., Montreal
Bruce Webster ..... 525 East 68 Street

DEATHS OF FELLOWS OF THE ACADEMY

Highman, Walter James, M.D., 853 Seventh Avenue, New York City; graduated in medicine from the College of Physicians and Surgeons, New York City, in 1905; elected a Fellow of the Academy January 6, 1910; died, January 24, 1934. Dr. Highman was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the American Dermatological Association, the New York Dermatological Society, the Pathological Society, the Society of Associated Alumni of Mount Sinai Hospital. He was Dermatologist to Mount Sinai Hospital and Associate Dermatologist to Lenox Hill Hospital.

McALPIN, DAVID HUNTER, B.A., M.A., M.D., Hotel McAlpin, Broadway and 34 Street, New York City; graduated in medicine from Bellevue Hospital Medical College, New York City, in 1888; elected a Fellow of the Academy April 4, 1895; died, January 20, 1934. Dr. McAlpin was a Fellow of the American Medical Association, a member of the County and State Medical Societies, the National Tuberculosis Association, the Pathological Society and the Society of Alumni of Bellevue Hospital.

BUREAU OF CLINICAL INFORMATION

The Committee on Medical Education maintains at the Academy a *Bureau of Clinical Information* where detailed information may be obtained regarding opportunities for postgraduate medical study in Greater New York and in other cities of the United States, Canada and Europe.

A survey of postgraduate medical education in New York City has constituted one of the important undertakings of the Committee since its organization in 1924. The survey has been carried on from year to year with a view to improving the value of existing opportunities and encouraging the development of additional ones. To attain this aim the Committee has given its approval to those courses which after investigation have been found to be well organized, with adequate equipment and clinical material, and given by physicians of character who are known to be qualified teachers in their special lines of work. The result of each year's survey has been the preparation and publication of a *Synopsis of Approved Postgraduate Medical Courses Offered in Greater New York.* Copies of the Synopsis may be obtained on application to the Bureau.

The meetings, lectures, conferences, hospital rounds, and other interesting medical activities of the day are announced in a *Daily Bulletin.* The Bulletin, which is issued the previous evening, also announces the major operative work to be performed in the clinics of most of the important hospitals of the city. A *Bulletin of Non-Operative Clinics* held in more than thirty hospitals also is published. Copies of these Bulletins may be obtained at the Bureau and will be mailed to visiting doctors on request.

The Bureau maintains an approved list of clinicians who practice in foreign countries, and is prepared to answer inquiries from physicians who desire information regarding foreign medical men engaged in general and special practice.

Physicians are invited to make the Bureau their headquarters while in the city.

Hospital Library

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- Hervey C. Williamson
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* Deceased.